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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,766	SLEPIAN, MARVIN J.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 6-37* is/are pending in the application.

4a) Of the above claim(s) *4,8-12,26,27,30 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,7,13-25,28,29,31 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to a response to an amendment filed 8/26/04. Claims 1, 3, 7, 13-17, 19, 24 and 25 have been amended. Claims 2 and 5 have been cancelled. Claims 34-37 have been added. Claims 4, 8-12, 26, 27, 30 and 32 have been withdrawn. Therefore, claims 1, 3, 6-7, 13-25 and 28, 29, 31 and 33-37 are under examination in this office action.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. The new grounds of rejection herein were necessitated by amendment and, therefore, this action is final.

Claim Objections

Claim 25 is objected to because of the following informalities: "wherein the means" is repeated twice. Appropriate correction is required. **This is a new objection necessitated by applicants' amendment.**

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6-7, 13-25 and 28, 29, 31 and 33-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection based upon applicants' amendment.**

The limitation that the agents are delivered in "a form (suitable) for local delivery" has been added to claims 1 and 25. Applicants have not indicated where support for this limitation is found. The examiner has been unable to find literal support in the originally filed specification for the term "form for local delivery". Therefore, the limitation of adding that the agents are delivered in "a form for local delivery" is impermissible NEW MATTER.

The limitation that the agents are delivered in "carrier selected from the group consisting of porous matrices, hydrogels.." has been added to claims 1 and 15. Applicants have not indicated where support for this limitation is found. The examiner has been unable to find literal support in the originally filed specification for the term "carrier" or for use of the listed polymers as a carrier. The specification teaches that polymers can be introduced into the endomural zone and that the polymers are bioactive themselves or contain bioactive materials. Firstly, it is not clear that this function is distinctly one of a carrier. Secondly, in the application as originally filed, the specifically recited polymers are therapeutic agents and not carriers. Therefore, the limitation of adding that the recited polymers are "carriers" is impermissible NEW MATTER.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 3, 6, 7, 13, 14, 25, 28, 29 and 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection based upon applicants' amendment.**

Claims 1 and 25 are vague and indefinite in that the metes and bounds of delivered in "a form (suitable) for local delivery" are unclear. While it appears as if a special step of preparing the agent for "local delivery" is required, the specification and the claims do not provide such as step. Therefore, it is unclear whether this form is *a priori* or a part of the method steps.

Claim 14 is vague and indefinite in that the metes and bounds of "first" are unclear. It is unclear to what the "first" refers. It appears from a reading of the specification that the cavity is formed prior to depositing the agents into the cavity as recited in claim 34, which implies that the cavity is formed "first" and the drugs deposited "second". However, claim 14 depends from claim 1, which do not recite a deposition in the cavity only steps of penetrating and entering and delivering of agents to the endomural zone.

Claim 35 is vague and indefinite in that the metes and bounds of "accessed" are unclear. It is unclear at what step the organ, organ component or tissue structure is accessed in claim 1 as claim 1 does not recite a step of accessing.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6-7, 13-15 and 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for delivering a therapeutic or diagnostic agent to the endomural zone, does not reasonably provide enablement for a method of treatment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This rejection is maintained for reasons of record in the office action mailed 10/4/04. The rejection has been slightly reworded based upon applicants' arguments. New claims 34-37 have been added to the rejection.**

1) Nature of invention. The invention recites a method of treatment comprising locally penetrating and entering the body of an organ, organ component or tissue structure with minimal damage to obtain access to endomural zones of the organ. Furthermore, drugs are deposited in the midzone of the organ. The invention utilizes disciplines of pharmacology, cell biology, medical technology and clinical techniques.

2) **Scope of the invention**. While applicants recite a method of treatment, no specific disease targets or means of treatment are taught. The broad and unspecific nature of the target diseases and means of treatment exacerbates the invention. Furthermore, the recitation that prophylactic agents are to be delivered exacerbates the unpredictable nature of the invention as applicants do not disclose prophylactic agents to be delivered nor disease to be prevented.

3) **Number of working examples and guidance**. The instant method is primarily directed towards a method of delivering agents into the endomural zone of an organ comprising penetrating and entering the endomural zone followed by delivering the agents. The endomural zone is described as the middle zone which comprises about 80% of the organ, organ component

or tissue structure. By organ component or tissue structure applicant refers to vessels or ducts. In a vessel for example, the endomural zone is also known as a lamina proper, submucosa, muscularis or media.

In the instant case, applicants propose methods and devices and kits directed toward delivery to the endomural zone with minimal collateral damage to healthy tissues or the target organ. Applicants provide three examples of devices that can be used to deliver agents to the endomural zone in figure 3, 4 and 5. These devices are comprised of hollow tubes such as catheters and delivery reservoirs filled with drugs, which are then expelled or dispersed into the endomural zone. The drugs are dispersed or expelled from the delivery means by an actuator, an activating or propelling agent or other means (see e.g. page 10, line 12-19). In addition the device can comprise sensors, guides, data storage etc (see e.g. page 10, line 20 through page 11, line 20). While the specification teaches multiple potential agents to deliver to "endomural zones", no specific targets or diseases to be treated are disclosed.

4) **State of Art**. The instant invention distinguishes itself from the prior art by specifically targeting the middle zone of an organ with drugs. In contrast the art is said to typically remove healthy or diseased tissue. Applicants propose use of devices, which are described as a hollow tube with a cutting or end penetrating means and a means of delivery to the endomural zone. Devices such as these appear to be well known in the art. Therefore, the instant invention advances the art by targeting specifically the endomural zone. However, it is not clear what step or part of the device delivers or targets the endomural zone specifically.

"Methods of treatment" are part of a high art. In order to treat a condition or disease, the disease must be known. This allows the target organ to be identified, the type and amount of

drug to be applied, treatment intensity and accompanying drug schedules. Similarly, the use of prophylactic agents is not accompanied by a disclosure in the specification as to the nature of the agents used to prevent disease nor what diseases are to be prevented.

5) **Unpredictability of the art**. The lack of disclosure of the recited methods steps coupled with the unpredictable nature of the art render the invention unpredictable for use in treatment protocols. The lack of disclosure as to types of diseases, therapeutic endpoints, time schedules of delivery or immune suppression exacerbates the unpredictable nature of the invention.

Furthermore, endomural is not commonly used to distinguish the "middle zone" of the tissue. As guidance, applicants have described the endomural zone to correspond roughly to the central 80% of these structures. For example, the heart does not appear to have an "endomural zone" as evidenced in the accompanying drawings in Ross (Composition of the Heart, online article June 1999). By deduction, it can be concluded that the myocardium can be considered the endomural zone of the heart. It is unpredictable that applicants' definition of the endomural zone can be properly deduced for every organ, organ component and tissue structure.

6) **Summary**. The invention recites a method of treatment, which is performed with a device that allows delivery of drugs to the endomural zone. The device is used to minimally cause damage to collateral tissues while allowing drugs to be deposited directly in the endomural zone. The unpredictability of using the claimed invention is accentuated due to the lack of methods or processes disclosed in the instant specification that exacerbate a highly unpredictable art.

In view of predictability of the art to which the invention pertains and the lack of guidance as to it use: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue unpredictable experimentation in order to practice the claimed invention.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 112, first paragraph on pages 10-12 of the amendment filed 4/4/05. Applicants argue that the state of the art is well established as surgical methods, percutaneous administration and such have been performed for years. Coupled with what applicants describe as examples of organs, organ components and tissues to be treated and methods and devices to use, the specification is said to not require undue experimentation.

Applicants' arguments filed 4/4/05 have been fully considered but they are not persuasive. The instant invention has been assessed completely as it relates to the prior art. However, whether an invention is enabled or not does not break down to the question of whether individual components or steps of the invention have the potential of operating as intended but rather if the invention as a whole will function as recited. The instant disclosure does not provide adequate guidance for those conditions to be treated that require penetration and entry and deposition of agents into the endomural zone. Furthermore, applicants have not provided

guidance as to the prophylactics to be used nor what diseases are to be prevented. Therefore, the instant invention cannot be performed with the recited broad scope of "method of treating".

The applicants' lack of guidance results in gaps in the method. Coupled with the unpredictable nature of the art, the method will not reliably allow treatment or preventive methods (as in the case of the prophylactive). This is not a question of experimentation as no amount of experimentation will generate the recited objective of treatment when no conditions are recited that are to be treated. The prior art does not teach methods of generic treatment or prevention. Rather the prior art teaches identification of a disease state followed by appropriate treatment protocols concerning drugs, schedule and means of assessing treatment. Therefore, the teaching of the specification and prior art do not teach one how to use the recited analysis for the detection of gene expression changes.

Summary of endomural zone

The instant specification has described the endomural zone as the middle zone of an organ, organ component or tissue structure. As guidance, applicants have described the endomural zone to correspond roughly to the central 80% of these structures. In the heart, the myocardium fits this description as evidence in the accompanying drawings in Ross (Composition of the Heart, online article June 1999). Specifically, as evidenced in the drawings depicting the layers of the heart, the endocardium and epicardium surround the myocardium. The myocardium is roughly 80% of the heart layer. In the spinal cord, the lateral corticospinal tract appears to be in the area of the spinal cord that can be considered the endomural zone as evidenced by William et al (The Human Brain: Dissection of the Real Brain, January 1997,

Chapter 1). Roughly 80% of the spinal cord is comprised of central cord, which encompasses the lateral corticospinal region (see figure).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 6, 7, 15-18, 20-23, 25, 28, 29 and 35-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Altman (US 6,585,716 B2; see entire document). **This rejection is maintained from the office action mailed 10/4/04. The rejection has been slightly reworded based upon applicants' arguments. New claims 35-37 have been added to the rejection.**

Altman teaches a drug delivery device for methods of treating the heart for injecting therapeutic agents into the myocardium. The method involves penetrating and entering the endomural zone (myocardium) with delivery of the agents to the endomural zone. Agents are delivered in microformulations such as microspheres (encompassing microcapsules and microparticles). The agents are delivered using a tubular "means for delivery", which is a means of delivery disclosed by the instant specification. The agents are in microspheres, which are locally delivered to the myocardium. Given the lack of disclosure as to the form the agents are in for "local delivery", the combination of the microspheres and drug delivery catheter would be said to place the agents in "a form for local delivery" as recited in claim 1. Drugs used include

growth factors and peptides and angiogenesis agents (see e.g. col 5, line 48-56 and col 4, line 1) or drugs as recited in claim 3, 6, 7, 28 and 29. The delivery device has a guidance system as recited in claim 23 and a hollow penetrating element i.e. a needle attached to a catheter as recited in claim 36 and 37 (see e.g. bridging paragraph col 3-4). The instant specification teaches that the means for creating a void can be a simple catheter or needle. Therefore, the needle of Altman et al can be used to create a void as recited in claim 15 and 25 and is comprised of metal as recited in claim 16. The catheter is flexible as recited in claim 17. Drugs are stored in a reservoir attached to the catheter and pumped automatically into the lumen of the drug delivery catheter through the penetrating element into the target (see e.g. col 5, line 15-39) as recited in claim 18, 21 and 22. Furthermore, sensors can be used with the device for electrical sensing (see e.g. col 5, line 65-67) as recited in claim 20. The delivery can be percutaneously or surgically (see e.g. col 5 , line 23-28) as recited in claim 35.

Claims 1, 3, 6, 7, 15-18, 19, 21-23, 25, 34, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Altman (US 6,102,887; see entire document). **This rejection is maintained from the office action mailed 10/4/04. The rejection has been slightly reworded based upon applicants' arguments and extended to claim 19. New claims 34, 36 and 37 have been added to the rejection.**

Altman teaches a drug delivery device for methods of injecting therapeutic agents into the myocardium through a distensible penetrating element with a chamber for holding the agent (se e.g. abstract). Specifically, the device is designed to penetrate the endocardium and inject drugs deep into the myocardium (see e.g. col 3, line 9-25). Agents are delivered in

microformulations such as microspheres or nanoparticles. The agents are delivered using a tubular "means for delivery", which is a means of delivery disclosed by the instant specification. The agents are in microspheres or nanoparticles, which are locally delivered to the myocardium. Given the lack of disclosure as to the form the agents are in for "local delivery", the combination of the nanoparticles and drug delivery catheter would be said to place the agents in "a form for local delivery" as recited in claim 1. Numerous agents are envisioned for delivery such as small molecules and macromolecules such as growth factors and polymers, which would fill the voids (see e.g. col 11 line 1 through 30 and figure 4a) as recited in claims 3, 6, and 7. The device comprises a penetrating end and is a hollow tube such as a needle (see e.g. col 4, line 11-12). Furthermore, an expansile cutter is included with the device. This expansile cutter is comprised of an expanding prong fixation that is sharpened to penetrate and spread the tissue (see e.g. col 9, line 22-44) as recited in claim 15, 19 and 25. The device comprises a needle and is thus comprised of metal as recited in claim 16. The drug delivery tube is comprised of a catheter and is thus flexible as recited in claim 17, 36 and 37 (see e.g. col 4, line 41-45) and is connected to reservoir (col 3, line 9-25) as recited in claim 18. Osmotic pumps or piston chambers drive drug delivery as recited in claims 21-23 (see e.g. col 6, line 40 through col 7, line 12) and is guided by a guiding catheter (see e.g. col 12, line 61-63) as recited in claim 23. The expansile cutters, create a void into which is deposited the agents for delivery (see e.g. col 10, line 48-54) as recited in claim 34.

Claims 1, 3, 6, 7, 14-16, 18, 20-24 and 34-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Haim et al, (US 6,309,370 B1; see entire document). **This rejection is maintained from the office action mailed 10/4/04. The rejection has been slightly reworded based upon applicants' arguments. New claims 34-37 have been added to the rejection.**

Haim et al teach an apparatus for intracardiac administration of growth factors into the myocardium (see e.g. abstract and col 3, line 24-42). Agents are delivered in microcapsules (see e.g. col 7, line 6-16). The agents are delivered using a catheter or tubular "means for delivery", which is a means of delivery disclosed by the instant specification. Given the lack of disclosure as to the form the agents are in for "local delivery", the combination of the microcapsules and drug delivery catheter would be said to place the agents in "a form for local delivery" as recited in claim 1. Growth factor drugs such as FGF or VEGF are envisioned for delivery (see e.g. col 9 line 4-10) as recited in claims 3, 6 and 7. The device comprises a laser beam that conveys a wave-guide to create channels into which the drugs are deposited (see e.g. col 5, line 20-21 and col 6, line 41-44) as recited in claims 14 and 34. The drug delivery device comprises a hollow needle, which is inserted into the heart with a laser beam that conveys a wave-guide to create channels or voids (see e.g. col 5, line 20-21 and col 6, line 41-44) as recited in claim 15. The device comprises a needle and is thus comprised of metal as recited in claim 16 and tubular as recited in claim 36. The device is connected to reservoir (col 13, line 1-15) as recited in claim 18 and delivered by pumps and is guided by a guiding catheter (see e.g. col 7, line 25-31) as recited in claims 21-23. A series of sensors for guidance, a position sensor and a optical sensor and one for identification of sites, a physiological sensor, a pressure sensor, an ultrasound sensor

(see e.g. col 3, line through col 6, line 28) as recited in claim 20, 24. The organ can be accessed percutaneously (see e.g. col 6, line 30-59) as recited in claim 35.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altman (US 6,585,716 B2; see entire document) or Altman (US 6,102,887; see entire document) or Haim et al, (US 6,309,370 B1; see entire document) in view of Benjamin and McMillan (Circ Res, 1998, Vol 83, pages 117-132; see entire document). **This rejection is maintained from the office action mailed 10/4/04.**

Applicants claim a method, devices and kits for treatment comprising locally penetrating and entering the body of an organ to gain access to an endomural zone. The device deposits drugs such as heat shock proteins (HSP) into the endomural zone.

The teachings of Altman, Altman and Haim et al are described above and are applied as before except; neither Altman, Altman and Haim et al teach use of heat shock proteins.

Benjamin and McMillan teach that HSP enhances the speed of recovery of the Ischemic Heart (see e.g. page 119, col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the drugs and growth factors taught by Altman, Altman and Haim et al

with the HSPs taught by Benjamin and McMillan because Altman, Altman and Haim et al et al teach that it is within the ordinary skill of the art to deliver drugs to the myocardium to treat cardiac vascular disease and because Benjamin and McMillan teach that it is within the ordinary skill of the art to enhance recovery of an ischemic heart with administration of hsps. One would have been motivated to do so in order to receive the expected benefit of improved myocardial function, preserved metabolic functional recovery, reduction of infarct size (see e.g. page 119, col 2). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brosamle et al (The Journal of Neurosciences, 2000, Vol 20:21, pages 8061-8068; see entire document) in view of Altman (US 6,585,716 B2; see entire document) or Altman (US 6,102,887; see entire document) or Haim et al, (US 6,309,370 B1; see entire document). **This rejection is maintained from the office action mailed 10/4/04.**

Applicants claim a method, devices and kits for treatment comprising locally penetrating and entering the body of an organ to gain access to an endomural zone. Applicants recite a use of kits comprising devices and a void filling material for nerve regeneration.

Brosamle et al teach the use of a device in which recombinant humanized IN-1 Fad antibody is delivered through by a pump through a catheter to the intrathecal space of the spinal cord. Specifically, a small hole in the dura matter was made and a catheter connected to a small osmotic pump was inserted into the subdural space close to the lesion (see e.g. figure 4).

Following administration of rIN-1 Fab induced regeneration of transected spinal cord axons was induced (see e.g. page 8065, col 1, paragraph 3).

Brosamle et al do not teach that the device has an end penetrating or cutting means with which the device is inserted into the endomural zone.

The teachings of Altman, Altman and Haim et al are described above and are applied as before.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the device and methods of treatment for nerve regeneration of Brosamle et al with the device of Altman, Altman and Haim et al because Brosamle et al teach that it is within the ordinary skill of the art to administer drugs through a catheter into the subdural space for infusion into a lesion and because Altman, Altman and Haim et al et al teach that it is within the ordinary skill of the art to use a drug delivery device that delivers drugs into the depths of the tissue. One would have been motivated to do so in order to receive the expected benefit of minimally invasive delivery of drugs in a local sustained manner for more effective drug effects (see e.g. US 6,309,370, col 2, line 50 through col 3, line 11). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants traverse the claim rejections under 35 U.S.C. 102 and 103 on pages 16-21 of the amendment filed 4/4/05. Applicants argue that Altman '716 and '877 do not disclose a

therapeutic agent that is in a form for delivery. Applicants further teach that the systems of Altman are easily removed from the site of administration. As well, applicants argue that neither Altman '716 or '877 nor Haim et al teach a means for creating a void and Haim does not disclose administering agents in a carrier. Finally applicants argue that Brosamle and Benjamin and McMillan do not cure the deficiencies.

Applicants' arguments filed 4/4/05 have been fully considered but they are not persuasive. The instant specification does not teach what form is required for local delivery. Given the unclear nature of this form, a person of skill in the art would predict that the form of Altman '716 and '877 are such that local delivery to the myocardium would be caused by use of microspheres or are nanoparticles, which contain the agents that are then delivered by catheter to the desired location. This combination of local delivery with microspheres or nanoparticles should be such that the agents are in a "form for local delivery". Haim et al teach us of microcapsules for delivery of agents to the target sites (see e.g. col 7, line 6-16) and therefore do anticipate the instant claims.

As to a means for creating a void, the instant specification teaches "Voids may be created by simple catheter, trochar or needle insertion." As well, the specification teaches that "(t)he void may be of identical size to the insertion device." (see page 11, line 22). Altman '716, Altman '877 and Haim et al teach use of a needle, while Altman '877 also teaches use of an expansile cutter. According to the disclosure, the means for creating a void is met by use of a needle. Therefore, Altman '716 and '877 and Haim et al by using the needle create a void that is the size of the needle. Finally, Brosamle and Benjamin and McMillan need not teach what the

primary references teach and thus need not teach a form for delivery, means for creating a void or carriers comprised of microcapsules.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

August 25, 2005

JAMES KETTER
PRIMARY EXAMINER